

## Effect of chitosan grafted polyethylenimine nanoparticles as a gene carrier on mesenchymal stem cells viability

Elham Malakooty poor<sup>1,2</sup>, Mohamadreza Baghaban Eslaminejad<sup>2,\*\*</sup>, Fatemeh Bagheri<sup>2,3</sup>, Esmail Mollarazi<sup>4</sup>, **Nematollah Gheibi<sup>1,\*</sup>**

<sup>1</sup>Cellular and Molecular Research Center, Qazvin University of Medical Sciences, Qazvin, Iran

<sup>2</sup>Department of Stem Cells and Developmental Biology at Cell Sciences Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran

<sup>3</sup>Department of Cell and Molecular Biology, School of Biology, University College of Science, University of Tehran, Tehran, Iran

<sup>4</sup>Department of Nuclear Pharmacy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

\*Corresponding Author: e-mail address: [gheibi\\_n@yahoo.com](mailto:gheibi_n@yahoo.com) (Nematollah Gheibi)

\*\*Co-Corresponding Author: e-mail address: [bagesla@yahoo.com](mailto:bagesla@yahoo.com) (Mohamadreza Baghaban Eslaminejad)

### ABSTRACT

This study discusses the effect of complexes of chitosan grafted polyethylenimine (Ch-PEI) with plasmid DNA on viability of mesenchymal stem cells (MSCs) derived from human marrow. Ch-PEI/pDNA nanoparticles were synthesized through the complex coacervation method using pIRES plasmid containing Green Fluorescent Protein (GFP) gene. To confirm the complexation, samples were run through an agarose gel. Human bone marrow mesenchymal stem cells were studied for the cytotoxicity of the nanoparticles by MTT assay. MTT results indicated Ch-PEI does not have any significant cytotoxicity compared with PEI and Lipofectamine<sup>2000</sup> leading to 40% cytotoxicity. According to the results it seems that grafting chitosan with PEI improves the MSCs viability.

**Keywords:** Chitosan; PEI; Cytotoxicity; Mesenchymal stem cell

### INTRODUCTION

Mesenchymal stem cells are clonogenic and nonhematopoietic cells in bone marrow with the ability of differentiating to different mesodermal cells such as osteoblast, chondrocyte and endothelial cells and even nonmesodermal cells such as neurons. They are the first stem cells used in clinical application because of their wide differentiating potential. Their low immunogenicity caused them to be used allogeneic [1]. Transfecting of some genes could lead to a better differentiation potential for example transfecting of TGF- $\beta$  gene could lead to chondrogenic differentiation or hTERT gene could enhance the proliferation [2,3]. But the important obstacle is the selection of the best procedure for gene transfection. In a perfect gene delivery system, the vector should be nontoxic and nonimmunogenic [4], should be small enough to enter nucleus [5].

Gene delivery vectors divide into two groups: Viral and nonviral but the simplest approach is

using of naked DNA. Direct injection of naked DNA in some tissues such as muscle shows a high level of expression [6]. Although it causes gene expression but its expression level is so less than viral or liposomal vectors. Transfection efficiency will be higher using viral vectors. But also there are some defects that limited their clinical application. The first and most important problem is patient's immunity [7]. Viral vectors could only transfer small sizes of DNA. They are mutagen and oncogen [8,9].

Nonviral vectors could be administered frequently with minimum immune response. Targetability, stability during storage and ease of production are some of their advantages [10]. Cationic lipids and cationic polymers are the two main types of nonviral vectors. They both interact negatively charged DNA with electrostatic bonds through their positive charge and compose complexes. Cationic polymers condense DNA and inhibit their degradation by nucleases. The most important feature is their low toxicity<sup>7</sup> but in